myocardial infarction who may in some respects differ from those studied in the GUSTO-1 angiographic trial.

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Protective Effect of Prodromal Angina Before Myocardial Infarction

In their recent report, Ishihara et al. (1) demonstrate that prodromal angina within 24 h of the occurrence of acute myocardial infarction exerts a protective effect on both early and long-term outcome. They also document a favorable trend for improved outcome in patients having angina at any time before their infarction. We feel that these results, observed in a comparatively young population (mean age <60 years), deserve a word of caution, emphasizing the possible confounding effect of age regarding the prognostic role of antecedent angina. In the same issue of the Journal, Abete et al. (2) justly pose the question of the possible lack of protective effect of previous angina in elderly patients (through the loss of the preconditioning mechanism in the aging heart): They show that hospital mortality was significantly lower in adults with (2.6%) than in those without (10%) antecedent angina, whereas no such trend was observed in elderly patients (≥65 years old) (in-hospital mortality: 14.4% vs. 15.2%, respectively). In a retrospective study of 151 patients ≥75 years old admitted for acute myocardial infarction (3), we found that the presence of antecedent angina was not related to in-hospital mortality (22% vs. 24%) but was indeed a marker of poor long-term outcome in this cohort (5-year probability of survival 69% in patients without vs. 38% in patients with antecedent angina), with a relative risk of 2.3 for patients with antecedent angina by multivariate analysis. We feel that this specific influence of antecedent angina in elderly patients developing acute myocardial infarction should be recognized because it seems to be an easy way to stratify patients at higher risk who might therefore need a specific diagnostic and therapeutic approach.

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Reply

We thank Danchin et al. for their interest in our recent study (1). In the study, we demonstrated that prodromal angina in the 24 h before infarction was associated with a lower in-hospital mortality rate and a better 5-year survival rate. As Danchin et al. pointed out, our study showed a trend for lower in-hospital mortality in patients having previous angina at any time. However, more important, if patients with prodromal angina in the 24 h before infarction were excluded from the group of patients with previous angina at any time, previous angina at any time no longer had the favorable effects: the in-hospital mortality rate was 12% in patients with previous angina at any time and 15% in those without angina ($p = 0.56$), and the 5-year survival rate was 72% and 74%, respectively ($p = 0.79$). We thus emphasize that only prodromal angina occurring shortly before the onset of infarction, but not previous angina at any time, has a favorable effect on outcome after infarction. Ischemic preconditioning is the potential mechanism by which prodromal angina acquires its protective effect. Previous angina itself, without an episode or episodes of ischemia occurring shortly before infarction, does not produce ischemic preconditioning.

The major point of issue raised by Danchin et al. is whether aging might lessen the protective effect of prodromal angina. To assess this issue, we performed additional analysis. When only 269 patients of age <70 years were compared, prodromal angina in the 24 h before infarction was associated with a lower in-hospital mortality rate (2.5% vs. 9.5%, $p = 0.03$) and a better 5-year survival rate (92% vs. 80%, $p = 0.01$). In turn, when 81 patients ≥70 years old were compared, prodromal angina in the 24 h before infarction did not affect the in-hospital mortality (26.5% vs. 25.5%, $p = 0.92$) and 5-year survival rates (40% vs. 55%, $p = 0.90$). The findings of our additional analysis on in-hospital mortality were comparable to those by Abete et al. (2) who demonstrated that the presence of angina before infarction was protective against in-hospital outcomes in adults, but such a favorable effect is less obvious in elderly patients. Our current analysis extended the findings of their study on in-hospital outcome to long-term outcome. The absence of preconditioning in elderly patients should be well recognized in assessing the implications of prodromal angina.

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